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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/586,326	06/07/2007	Shigeru Kinoshita	80183(305882)	1834
21874	7590	06/15/2011	EXAMINER	
EDWARDS ANGELL PALMER & DODGE LLP			WESTERBERG, NISSA M	
P.O. BOX 55874			ART UNIT	PAPER NUMBER
BOSTON, MA 02205			1618	
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>
	10/586,326	KINOSHITA ET AL.
	<b>Examiner</b>	<b>Art Unit</b>
	NISSA WESTERBERG	1618

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

#### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

1) Responsive to communication(s) filed on 29 April 2011.  
 2a) This action is **FINAL**.                    2b) This action is non-final.  
 3) Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

4) Claim(s) 1-8 and 11-17 is/are pending in the application.  
 4a) Of the above claim(s) 1-4, 11-14 is/are withdrawn from consideration.  
 5) Claim(s) \_\_\_\_\_ is/are allowed.  
 6) Claim(s) 5-8 and 15-17 is/are rejected.  
 7) Claim(s) \_\_\_\_\_ is/are objected to.  
 8) Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

9) The specification is objected to by the Examiner.  
 10) The drawing(s) filed on \_\_\_\_\_ is/are: a) accepted or b) objected to by the Examiner.  
 Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
 Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).  
 11) The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

12) Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).  
 a) All    b) Some \* c) None of:  
 1. Certified copies of the priority documents have been received.  
 2. Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.  
 3. Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

<b>Attachment(s)</b>	
1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.	4) <input type="checkbox"/> Interview Summary (PTO-413) Paper No(s)/Mail Date. _____. 5) <input type="checkbox"/> Notice of Informal Patent Application 6) <input type="checkbox"/> Other: _____.

## DETAILED ACTION

### ***Response to Arguments***

1. Applicants' arguments and amendment, filed April 29, 2011, have been fully considered but they are not deemed to be fully persuasive. In view of the amendments to the claims, the rejection under 35 U.S.C. 103(a) as being unpatentable over Rossi et al. in view of Brodnitz et al. is withdrawn. A new ground of rejection is set forth below.

### ***Claim Rejections - 35 USC § 103***

2. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

3. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

4. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 5 – 8, 15 and 16 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossi et al. (Curr Eye Res, 1990) in view of Brodnitz et al. (J Agr Food Chem, 1971), Kobe (US 1,993,610) and Jarvenpaa et al. (Z Lebensm Unters Forsch A, 1998).

Rossi et al. investigates the use of the substance eledoisin as a possible treatment for dry eye (abstract). Average basal tear flow was measured prior to application of eledoisin to the eye by collection of fluid from the cannula (p 274, col 1, ¶ 2) to provide an initial tear volume measurement step. Eledoisin was applied to the eye, resulting in exposure of the eye to the potential lachrymator substance, and two more tear volume measurements, corresponding to the first and second 10 minute time period following exposure, were performed (p 274, col 1, ¶ 2). In a separate set of experiments, the wetting of a sponge was used to measure tear volume before and after exposure of the eye to eledoisin (p 274, col 1, ¶ 4).

Rossi et al. does not disclose the use of the thioalkanal-S-oxide compounds required in the instant claims.

Brodnitz et al. discloses that thiopropanal S-oxide (a compound according to claim 1 in which R is a C<sub>1</sub> alkyl) is the lachrymatory factor in onions (abstract). A series of straight chain thioalkanal S-oxides that were synthesized also possess lachrymogenic properties (p 272, col 1, ¶ 2). These compounds correspond to the compound in claim 1 with R being C<sub>1</sub>, C<sub>2</sub> or C<sub>3</sub> alkyl chain (Table III, p 271).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to use a thioalkanal S-oxide as the tear producer reagent in the method taught by Rossi et al. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success because Brodnitz et al. discloses that thioalkanal S-oxides are the compounds found in onions that are responsible for the stimulation of tear production. Measurement of the tear volume before and after exposing the eye of a subject to a substance known to induce tear production (lachrymation) allows the determination of the relative strength of the lachrymation effect and/or effective dose of the lachrymator compound for increasing tear production. Information about the effective dose and exposure time required to induce tear formation would provide information to the practitioner of the amount of time that the thioalkanal S-oxide must be exposed to the eye in order to have the effect, which reads on the stimulation measurement step of claim 6.

Rossi et al. topically applies the eledoisin to the eye in order to stimulate tear production as does not disclose a non-contact manner as required by the instant claims.

Kobe discloses a composition for producing lachrymating gases that cause irritation to membranes including the eyes, leading to uncontrolled tearing (col 1, 1 – 7). This is achieved through the use of volatile compounds (col 1, ln 33 – 40). These gases induce lachrymation in a non-contact manner as the components need not be directly applied to the eye. The contact of the compound in the gas phase with the eye leads to tearing.

Jarvenpaa et al. discloses that at 1 minute after cutting of an onion, thiopropanal-S-oxide was the most abundant compound of the volatile compounds in yellow onions (abstract; p 40, col 2, ¶ 2).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to expose the eye in a non-contact manner using the volatile compound thiopropanal-S-oxide. The person of ordinary skill in the art would have been motivated to make those modifications and reasonably would have expected success because Jarvenpaa et al. demonstrates that thiopropanal-S-oxide is volatile and Brodnitz teaches that this compound is lachrymatory compound, while Kobe et al. discloses that volatile compounds can stimulate irritation and tearing without direct physical stimulation to the eye. Given this effect and the desire of other people, e.g., the doctor or other personnel, in the room to not experience the same tearing effect, it would also be obvious to place the thiopropanal -S-oxide in the region of the eye in a confined space, such as a container, to expose the eye of the subject to the lachrymator substance without exposing others. Unlike liquids administered directly to the eye, the

volatile gas would expand throughout the room if not confined by a container of some sort.

6. Claim 17 is rejected under 35 U.S.C. 103(a) as being unpatentable over Rossi et al. in view of Brodnitz et al., Kobe and Jarvenpaa et al. as applied to claims 5 – 8, 15 and 16 above, and further in view of Tompkins et al. (J Insect Physiol, 1980).

As discussed in greater detail above, the combined references teach that thioalkanal-S-oxides such as thiopropanal-S-oxide are volatile, lachrymatory substances. Such substance can induce tearing and need not be placed in direct contact with the eye in order to elicit tearing. These gases can be contained and only administered to the subject through the use of a container filled with the volatile compound as otherwise, other people in the room/area would also be exposed.

None of the references explicitly disclose the reagent on filter paper being placed inside the container.

Tompkins et al. prepared samples of volatile compounds from various sources (p 690, col 1, ¶ 4) and tested the effects of the volatile compound on the courtship behavior of various populations of fruit flies (p 691, col 1, ¶ 3). After dilution of the extract with a volatile solvent, the solution was applied to filter paper squares placed inside a chamber (p 691, col 1, ¶ 3 - col 2, ¶ 2).

It would have been obvious to the person of ordinary skill in the art at the time the invention was made to apply the volatile lachrymatory compounds to filter paper that is then placed inside the exposure container. The person of ordinary skill in the art would

have been motivated to make those modifications and reasonably would have expected success because Tompkins et al. discloses such steps for exposing organisms to volatile compounds. Placing the volatile liquid directly in the container could lead to inadvertent contact of the solution with the subject as the liquid flows around the container depending on the length of time it takes for the volatile solution to evaporate. If the solution is instead soaked into the filter paper, no free flowing liquid is present in the container.

***Conclusion***

7. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NISSA WESTERBERG whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8:00 a.m. - 4 p.m. ET.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Nissa M Westerberg/  
Primary Examiner, Art Unit 1618